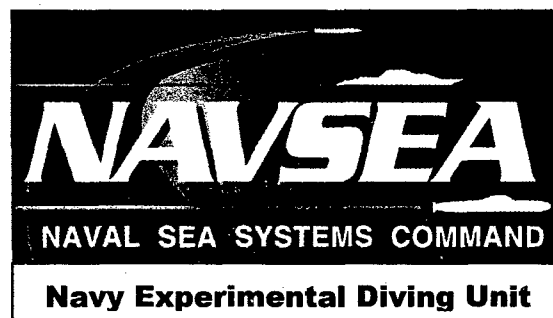


Navy Experimental Diving Unit
321 Bullfinch Rd.
Panama City, FL 32407-7015

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NEDU TR 05-21
November 2005

**TWO CONSECUTIVE FIVE-DAY WEEKS OF
DAILY FOUR-HOUR DIVES WITH
OXYGEN PARTIAL PRESSURE 1.4 ATM**



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Author: B. Shykoff, Ph.D.

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19. ABSTRACT Sixteen U.S. Navy divers began a series of 4-hour dives at a Po ₂ of 1.4 atm daily for two consecutive five-day weeks. Nine divers were able to finish; all withdrawals were for nonpulmonary reasons. Divers rested on the bottom of a 15-foot fresh water pool and breathed humidified 100% oxygen open circuit from MK 20 full face masks. Flow-volume curves and diffusing capacity were measured at baseline, daily during diving, and after the series. Symptoms and changes in pulmonary function values were used to measure pulmonary oxygen toxicity, and the results were compared to earlier series of similar four-hour dives. During the two weeks of daily diving, one subject showed progressive pulmonary symptoms that increased from mild to moderate. All other symptoms and all pulmonary function changes were rated as mild. From these data and those gathered after other similar dives, we find no evidence of general accumulation of toxicity, though flow-volume changes are more common after two consecutive dives than after one. Diffusing capacity changes are sufficiently infrequent to be difficult to characterize. After any 4-hour, 1.4 atm oxygen dive, 17% of divers may report symptoms, and no more than 18% are expected to show changes in flow-volume parameters.				
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CONTENTS

	<u>Page No.</u>
DD Form 1473	i
Contents	ii
Introduction	1
Methods	1
General	1
Experimental Design and Analysis	3
Equipment and Instrumentation	3
Procedures	3
Results	4
Discussion	9
Conclusions	13
References	14

TABLES

Table 1: Subject characteristics	2
Table 2: Symptoms list	3
Table 3: Pulmonary function depression and symptoms after the dives	5
Table 4: Incidences of pulmonary toxicity as a function of the number of dives	10

FIGURES

Figure 1: Changes in pulmonary function over time for Subject 5	6
Figure 2: Changes in diffusing capacity over time for Subject 1	7
Figure 3: Changes in diffusing capacity over time for Subject 9	7
Figure 4: Changes in pulmonary function over time for Subject 8	8
Figure 5: Changes in FVC with increasing number of dives	11
Figure 6: Changes in FEV ₁ with increasing number of dives	11
Figure 7: Changes in FEF _{max} with increasing number of dives	12
Figure 8: Changes in FEF ₂₅₋₇₅ with increasing number of dives	12
Figure 9: Changes in D _L CO with increasing number of dives	13

INTRODUCTION

The *U.S. Navy Diving Manual* authorizes divers to breathe oxygen for up to 240 minutes per day at depths of 20 feet of seawater (fsw) or less.¹ However, the testing on which this limit is based was conducted as single exposures.² Because the first Navy Experimental Diving Unit (NEDU) testing that was designed specifically to study pulmonary oxygen toxicity showed that some symptoms or changes in pulmonary function first appeared one or two days after the oxygen exposure,³ we were concerned about possible cumulative injury. We looked first for any accumulation of injury after two or five consecutive days of diving⁴ and then extended that investigation to two five-day weeks of daily diving, as specified in the task *Pulmonary Oxygen Toxicity after Repeated Diving with Elevated Oxygen Partial Pressures*.⁵

Dives were synchronized to time of day and thus occurred with 20-hour surface intervals on weekdays. We measured changes in pulmonary function and assessed symptoms immediately and for several days after the exposures. The pulmonary function variables determined from forced flow-volume loops were forced vital capacity (FVC), forced expired volume in one second (FEV₁), peak expired flow or maximum forced expired flow (FEF_{max}), and average forced expiratory flow from 25% to 75% of expired volume (FEF₂₅₋₇₅). Diffusing capacity of the lung for carbon monoxide (D_LCO) was determined from single breath tests. The lower limits of normal for pulmonary function variables were defined as decreases from baseline of 2.4 times the coefficient of variation (cv) found for the NEDU population — namely, 7.7% for FVC, 8.4% for FEV₁, 16.8% for FEF_{max}, 17.0% for FEF₂₅₋₇₅, and 14.2% for D_LCO.³ We defined decreases of these magnitudes, the lower 95% confidence bands for each variable, as the lower limits of normal.

Because we had seen hyperoxic myopia after a series of five six-hour dives,⁶ we measured visual refraction daily. In addition, divers had complete eye examinations at the Tyndall Air Force Base Optometry Clinic before and after the dive series.

METHODS

GENERAL

We recruited 16 divers for this study. During the dives, subjects rested on the bottom of NEDU's fifteen-foot-deep test pool in comfortably warm water (90 ± 5 °F; 31 ± 3 °C), where they breathed humidified 100% oxygen open circuit from the MK 20 underwater breathing apparatus. For a diver whose regulator was under 10 feet of water (standing on the bottom), the oxygen partial pressure (P_{O₂}) would have been 1.3 atmospheres (atm), and for whose regulator was under 14 feet of water (lying on the bottom), the P_{O₂} would have been 1.4 atm. Divers were usually seated, either on plastic chairs, for P_{O₂} of 1.3 atm, or on the bottom, for P_{O₂} of 1.4 atm. Divers were permitted to surface and breathe room air for five minutes in every hour, when they could eat or drink.

Before the study, subjects had not been diving while breathing air or mixed gas for one week or while breathing oxygen for two weeks. Except for the experimental dives, they

refrained from diving throughout the testing period. Each subject's smoking behavior and history of respiratory allergies were noted, and subjects' general health and use of medications also were recorded during the studies. All subjects were in good health.

Table 1.
Subject characteristics.

	Median (range)	
Age (Yr)	36	(28–49)
Height (in)	69.5	(66–74)
Weight (lb)	190	(150–265)
Smoking: (#)	<i>never</i> , 9; <i>former</i> , 5; <i>current</i> , 2	
Respiratory allergies (#)	3	(None active)
Anti-inflammatory medication (#)	3	

Each session to measure pulmonary function involved acquiring three flow-volume loops, with the tests performed and repeatable according to American Thoracic Society standards.⁷ FVC, FEV₁, FEF_{max}, and other variables were read from the flow-volume loops. The sessions also included three single-breath D_LCO measurements made with a 10-second breath hold. The variables used to obtain D_LCO were calculated from the gas concentrations before and after the breath hold. Adjustments were made for carboxyhemoglobin and hemoglobin concentrations,⁸ and the samples were chosen to ensure that the analyzer signal was stable when measurements were recorded.⁹

Baseline pulmonary function tests (PFTs) were done three to five days before the test dives and, for flow-volume tests, also immediately before diving. The averages of three technically correct diffusing capacity tests and of three properly-performed flow-volume loops from both sessions were used for comparisons with later values. During the weeks of diving, measurements of flow-volume loops were made in the morning before each dive; any diver with FVC or FEV₁ less than twice the confidence interval below baseline was to have discontinued diving in the series. Both flow-volume curves and diffusing capacities were measured within an hour of surfacing, for two days after an early termination of the series, and on the Monday and Tuesday after the final dive. If FVC, FEV₁, FEF_{max}, or D_LCO was considered to be different from baseline, the measurement was repeated until pulmonary function was seen to be restored.

Visual refraction was measured at each session measuring pulmonary function and one week after the end of the series, as well as during the eye examinations at the optometry clinic. Divers were not permitted to continue in the series if refraction in the morning had decreased from baseline by 0.5 diopters (D) or more. Divers with a refractive shift were checked in the laboratory daily until the change had resolved, and they were referred to the eye clinic as soon as possible.

Divers were questioned about specific symptoms (Table 2) each hour during the dive and at each session measuring pulmonary function.

Table 2.
Symptoms list.

During the dives:	After the dives:
Vision changes	
Ringing or roaring in ears	
Nausea	
Tingling or twitching	
Light-headedness or dizziness	
Chest tightness	Chest pain or tightness
Shortness of breath	Shortness of breath
Rapid shallow breathing	
Inspiratory burning	Inspiratory burning
Cough	Cough
	Visual complaints
	Ear problems
	Unreasonable fatigue
	Lowered exercise tolerance

EXPERIMENTAL DESIGN AND ANALYSIS

Pulmonary function variables were considered to be different from baseline if they were outside the 95% confidence bands. Confidence in estimates of the incidence of changes in pulmonary function or of symptoms was obtained from the binomial distribution. Magnitudes of changes and any other effects are described in **RESULTS** below.

EQUIPMENT AND INSTRUMENTATION

The Collins CPL and Collins GS Modular Pulmonary Function Testing System instruments (Ferraris Respiratory; Louisville, CO) were used to measure pulmonary function. The test gas used to measure D_LCO contained 0.3% CO and 0.3% methane. A CO oximeter (Instrumentation Laboratory; Lexington, MA) determined the pretest carboxyhemoglobin and hemoglobin concentrations from a venous blood sample. Humidifiers (bubblers) built at NEDU for the purpose were connected in the gas circuits at the test pool.

PROCEDURES

Eight divers began each set of dives. Every workday morning for two weeks, divers reported to the laboratory and, dressed for comfort, were directed to enter the water at about 10-minute intervals after they had completed their pre-dive measurements. The 4-hour period started when they began to breathe oxygen. Divers settled on the bottom to relax and watch movies.

Divers surfaced sequentially at the ends of their dives and were escorted to the laboratory for blood draws, for testing of pulmonary function and visual refraction, and for recording of symptoms. On the days after diving, the measurements were repeated.

RESULTS

All respiratory results are shown in Table 3, where subjects have been assigned arbitrary numeric identifiers. Only nine subjects were able to complete the dive series, but none of those who did not complete the series withdrew because of pulmonary function changes. One subject (Subject 16 in Table 3) became ill after completing two dives. Three subjects had to stop diving because of corneal abrasions; Subject 13 was injured in a sports accident, and Subjects 11 and 14 were injured possibly by ill-fitting contact lenses worn during the first dives; one had a tear in a soft contact lens, and the other had been advised at his pre-dive optometry appointment that his gas permeable lenses were warped. Three subjects—Subjects 10, 12, and 15—were required to stop diving because their visual refractions had shifted by -0.5 D from baseline, but all visual changes had resolved by the next measurement session, and no significant changes were found in their postdive optometry examinations.

PULMONARY FUNCTION AND RESPIRATORY SYMPTOMS

Eight divers had measurable deficits in pulmonary function variables, and three divers reported symptoms. None of the subjects reported symptoms simultaneous with a change in pulmonary function. Time courses of changes for some subjects, selected to show the types of responses observed, are shown in Figures 1–4.

Pulmonary function changes were scattered across dive days, and those evident early in the dive series often resolved as diving continued. Even when changes were not significant, the values were not absolutely steady; Figure 1 shows a fairly common pattern of fluctuation in flow-volume parameters about a mean value.

To look for trends, linear regressions for percentage differences from baseline against dive number were calculated. For flow-volume parameters, at least one slope differed from zero in five of the ten subjects who completed at least eight dives, but the average slopes were not significantly different from zero. Two subjects showed significant positive slopes: Subject 1 in FVC, FEV_1 , FEF_{max} , and FEF_{25-75} , and Subject 9 in FEF_{25-75} . Subject 7 showed an apparent decrease in FVC with time because of low baseline values and high readings after the first dive; most measured values were above baseline. Subject 8 showed a significant decrease in FVC with time [$-0.3\%/day$, standard error of slope (SE) 0.1% ; $p < 0.001$] (Fig. 4), and Subject 10 showed significant decreases in FEV_1 ($-0.6\%/day$, SE $0.1\%/day$; $p < 0.001$) and FEF_{25-75} ($-1.6\%/day$, SE $0.4\%/day$; $p < 0.002$) with number of dives. For D_LCO , slopes were significantly less than zero in five subjects and greater than zero in none: Regression slopes, standard errors, and significance values were $-0.9\%/day$, SE $0.1\%/day$, $p < 0.001$; $-0.8\%/day$, SE $0.3\%/day$, $p < 0.03$; $-0.6\%/day$, SE $2\%/day$, $p < 0.03$; $-1.4\%/day$, SE $0.2\%/day$, $p < 0.001$; and $-0.8\%/day$, SE $0.3\%/day$, $p < 0.02$ for Subjects 2, 3, 6, 7, and 8, respectively. The average slope of D_LCO vs. dive day for the ten divers was $-0.6\%/day$.

Table 3.

Pulmonary function depression and symptoms after the dives.

ID	Dive Number										Post
	1	2	3	4	5	6	7	8	9	10	
1	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-	i	-
3	-	-	-	midF 19.1%	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-	-	-
5	-	-	midF 17.8%	-	-	-	-	FVC 8.6% FEV ₁ 8.9%	-	-	-
6	-	FEV ₁ 9.7%	-	-	-	-	s	-	D _L CO 17.9%	D _L CO 17.3%	-
7	-	-	-	-	-	D _L CO 14.9%	-	-	D _L CO 16.7%	D _L CO 15.4%	-
8	-	-	-	c	i, c	i, h	i, c, h	i, c, t, h	h	i, h	i, h
9	-	-	-	-	-	-	-	-	D _L CO 16.8%	-	-
10	-	-	-	-	-	midF 18.3%	-	-			midF 23.7%
11	-	-	-	FVC 9.0% FEV ₁ 10.2% F _{max} 20.2%	-						F _{max} 18.7%
12	-	midF 24.9%	midF 18.4%	midF 32.8%	midF 27.8%						midF 32.5%
13	-	-	-								-
14	-	-									-
15	FVC 9.9%	-									
16	-	-									

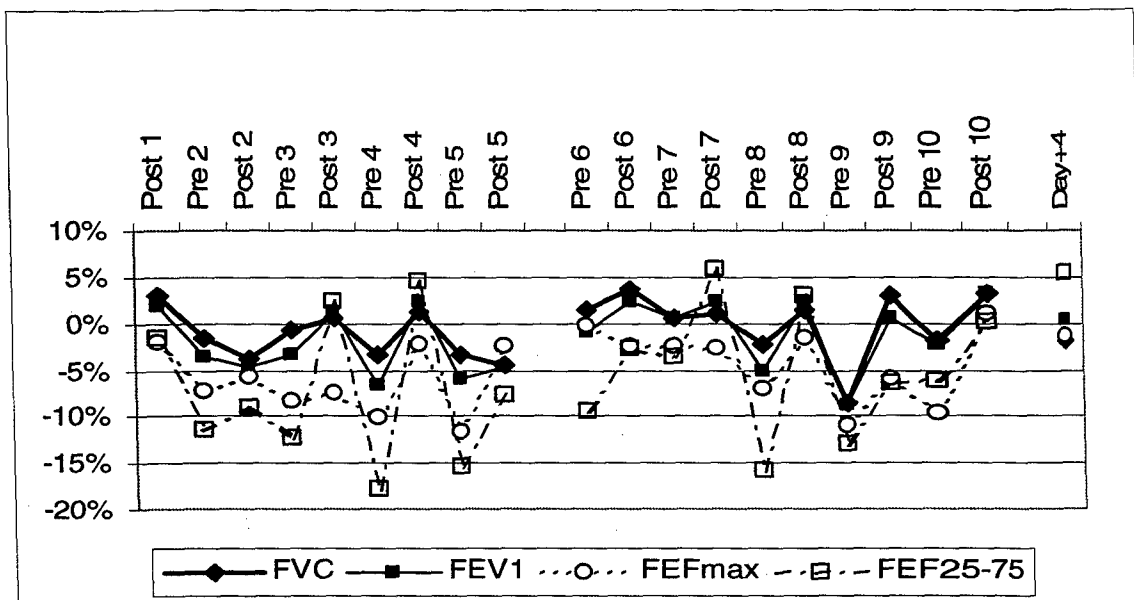
Values indicate the most severe occurrence for the time interval where, for example, "3" means from the start of Dive 3 until the start of Dive 4, and "Post" refers to all measurements taken days after the dive series.

Abbreviations: "midF" is FEF₂₅₋₇₅, "F_{max}" is FEF_{max}, "i" is inspiratory burning, "c" is cough, "t" is chest pain or tightness, "s" is scratchy throat, and "h" is hoarseness.

Boldface represents moderate symptoms, while others are mild symptoms. Grayed boxes indicate that the subjects aborted the dive series. (See the text for reasons for their terminations.)

None of the signs and symptoms listed was associated with a respiratory infection.

a)



b)

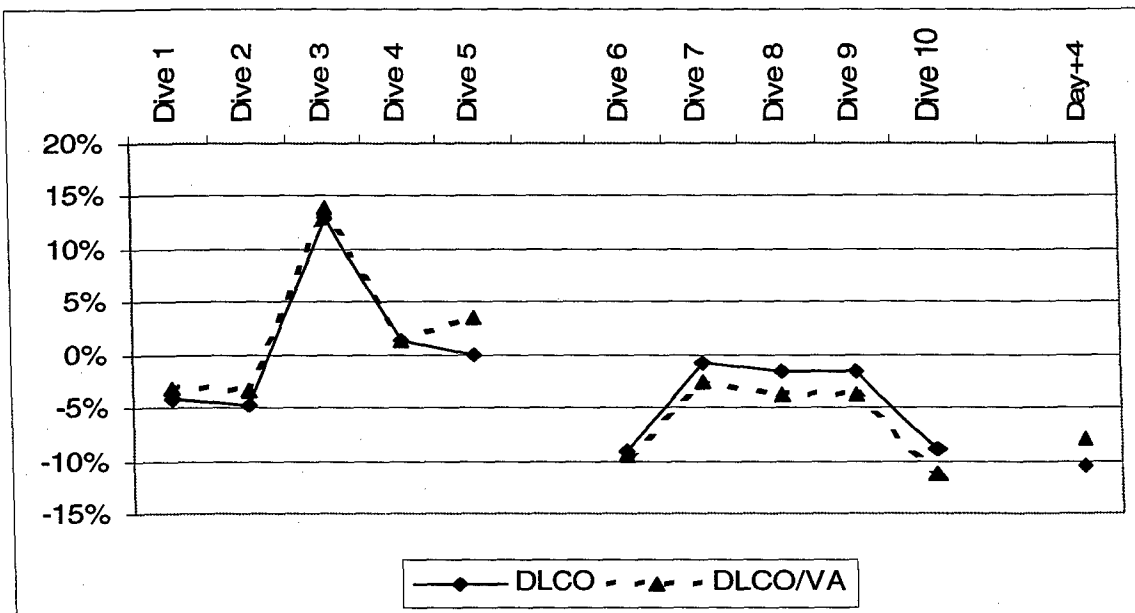


Figure 1. Changes in pulmonary function over time for Subject 5.

a) Flow-Volume. Oscillations in FEF_{25-75} and FEV_1 (with the lower values occurring in the morning after a dive the day before, and improvements becoming evident after the next dive) also were seen in other subjects, but oscillations with opposite phase or absence of oscillation were also seen.

b) Diffusing capacity. V_A is alveolar volume during the breath hold. The apparent increase after Dive 3 helps illustrate that values vary both ways around baseline.

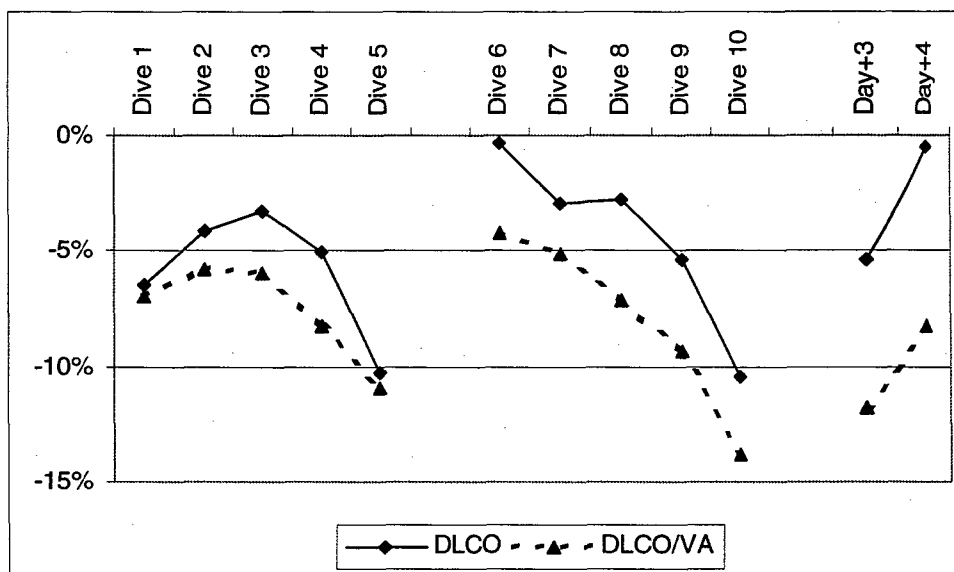


Figure 2. Changes in diffusing capacity over time for Subject 1. V_A as in Figure 1. This tracking looks like a slow deterioration from Dives 3 to 5 and again from Dives 6 to 10, with recovery on days without dives. Linear slopes for dives 1–5 are not significantly different from zero, but for dives 6–10 the slopes are D_LCO : $-2.3\%/day$, $p < 0.02$; D_LCO/V_A : $-2.4\%/day$, $p < 0.01$.

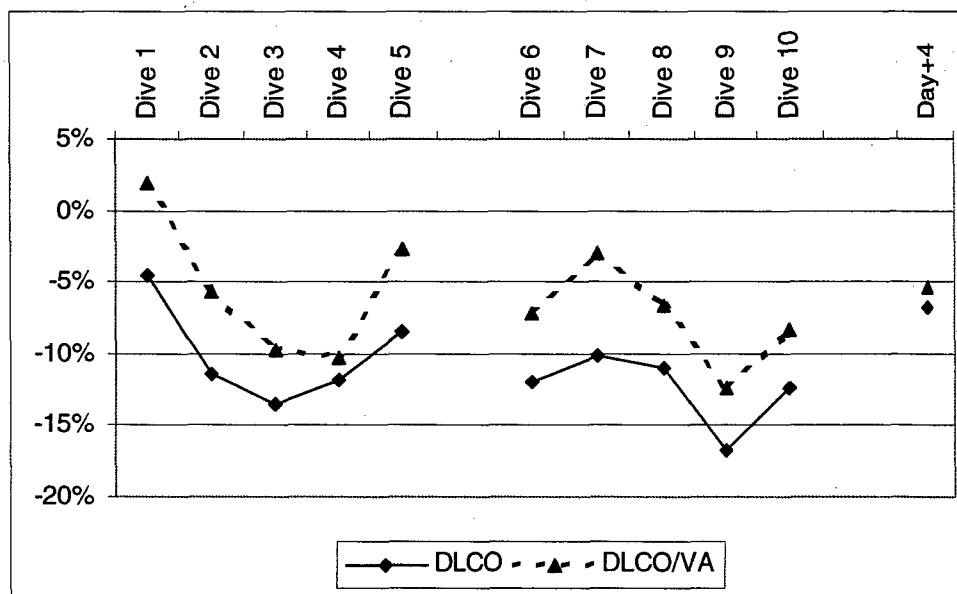
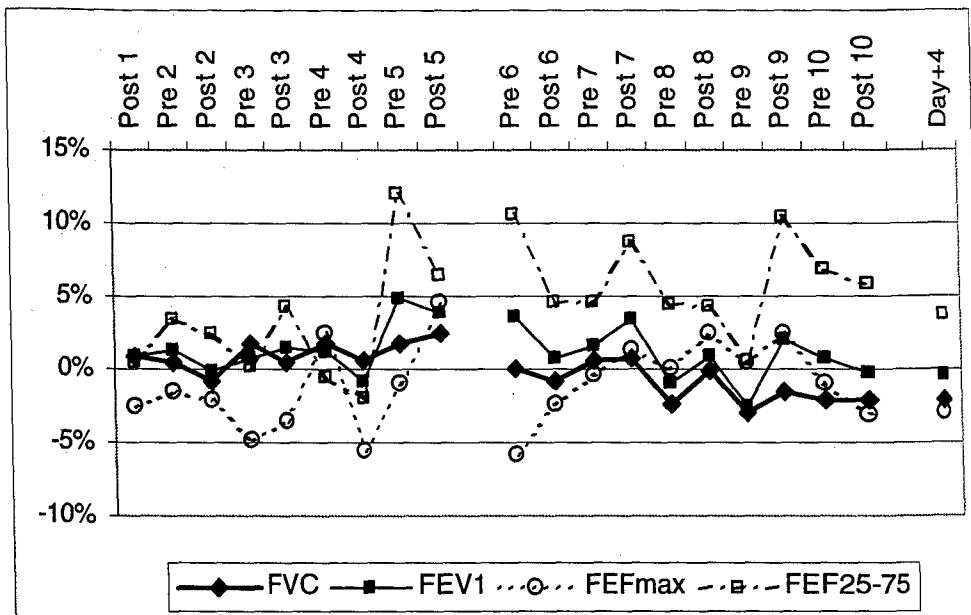


Figure 3. Changes in diffusing capacity over time for Subject 9. V_A as in Figure 1. Note that increases occurred while diving continued. Linear slopes for all segments are not significantly different from zero.

a)



b)

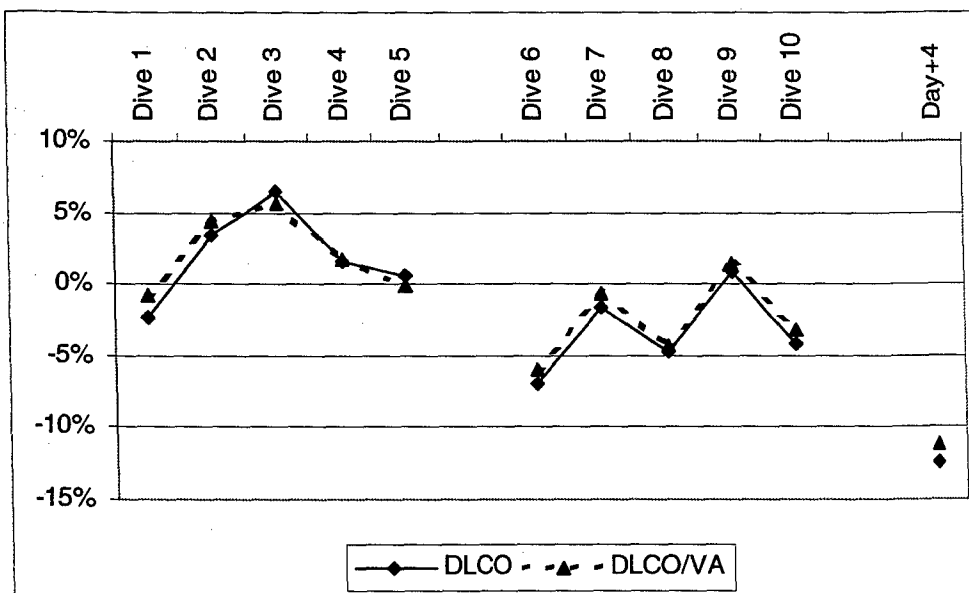


Figure 4. Changes in pulmonary function over time for Subject 8. This was the subject with symptoms throughout the second week.

- a) Changes in Flow-Volume Parameters. Slope of FVC vs. time during the second week is $-0.6\%/day$ ($p < 0.03$). Other slopes do not differ from zero.
- b) Changes in Diffusing Capacity. V_A as in Figure 1. Neither dive period had a slope significantly different from zero, but the overall slope including Day+4 was negative ($p < 0.02$).

Only Subject 8 demonstrated cumulative effects of these dives, and only for symptoms. However, although his pulmonary function changes were always within the limits of normal, as noted above, his FVC showed a significant trend downward (Fig. 4). This diver's symptoms (Table 3) were more persistent as the dive series continued. After Dives 6 through 8, his inspiratory burning and hoarseness resolved after five to six hours, but he was still hoarse on the morning of Dive 10, and after Dive 10 his symptoms persisted for a full day.

OTHER SYMPTOMS AND SIGNS

No subject reported exercise intolerance or unusual fatigue after these dives. Three divers — Subjects 6, 7, and 9 — reported symptoms of middle ear gas absorption (Draeger ear) after at least one dive. In Subject 4 after three dives, and in Subject 15 after one dive, we measured increases in hemoglobin concentration of more than 10%, indicative of dehydration. No subject showed visual changes that could be attributed to hyperoxic myopia after these dives, although one subject had persistent and significant myopic changes related to corneal abrasion.

DISCUSSION

A major difficulty in assessing this long, manpower intensive dive series is that illness and injury reduced the subject pool. We also reduced the number through what now appears to have been an overly strict limit on refractive change; in future work we will propose that these limits be relaxed. With only nine subjects completing the test, lack of statistical significance could easily be attributed to small number. However, if we examine the incidences after all 4-hour dives we have conducted at this P_{O_2} ,⁴ we can look for the influence of increasing numbers of 4-hour dives on pulmonary oxygen toxicity.

We have reported previously on 59 divers who completed at least one 4-hour dive with oxygen partial pressure 1.35 atm, 33 divers who completed at least two dives in a row, 17 who completed at least three consecutive dives, 17 who completed at least four, and 16 who completed at least five dives.⁴ In this study we added additional divers, reaching the totals shown in Table 4, where, for each dive number, we list overall incidences of symptoms within the 24 hours after a dive begins, measured differences within the 20 hours after a dive surfaces, and binomial 95% confidence intervals around the incidences.

The incidence of symptoms remained steady with increasing numbers of dives; all values found lie within the confidence interval for the incidence after a single dive. Furthermore, the linear regression of incidence vs. dive number yields a slope not different from zero. The best estimate for incidence of symptoms after any 4-hour dive with P_{O_2} of about 1.4 atm is that obtained with most divers, or 16.9% after a single dive. The overall incidence, the total number of subject-days with symptoms reported divided by the accumulated number of diver opportunities to report symptoms (the total of the second column in Table 4), is 16.3%.

Table 4.

Incidences of pulmonary toxicity as a function of the number of dives.

# dives, n_d	# divers who completed at least n_d dives	Incidence of symptoms	Incidence of flow-volume changes	Incidence of D_LCO change
1	75	16.9% (9–27%)	5.2% (1–13%) * ^b	0
2	49	13.7% (6–26%)	17.6% (8–31%) * ^a	3.9% (0.5–15%) [†]
3	30	20.0% (8–38%)	3.3% (0.1–17%) ^a	0
4	29	20.7% (8–40%)	13.8% (4–32%) ^b	0
5	28	17.9% (6–37%)	3.6% (0.1–18%)	0
From Table 3, for comparison:				
6	10	10.0% (0.2–45%)	0	10.0% (0.2–45%)
7	10	10.0% (0.2–45%)	0	0
8	10	10.0% (0.2–45%)	10.0% (0.2–45%)	0
9	9	11.1% (0.3–48%)	0	33.3% (7–70%) [†]
10	9	22.2% (3–60%)	0	22.2% (3–60%)

Values in parentheses are binomial 95% confidence intervals. Pairs under scrutiny are indicated by matching superscripts, as below.

* Pair differs: $p < 0.03$ by one-tailed Fisher's Exact Test; $p < 0.04$ by two-tailed.

[†] Pair differs: $p < 0.03$ by Fisher's Exact Test, one- or two-tailed.

Pairs do not differ by Fisher's Exact Test. ^a $p > 0.05$; ^b $p > 0.1$

The incidence of a decrease greater than normal variability in any flow-volume parameter was significantly higher after two dives than it was after one, but this may be an artifact caused by dichotomizing a continuous difference from baseline into groups above or below a threshold; severity of change was not different, as shown in Figure 5. Although the apparent incidences (Table 4) fluctuated as the number of dives increased beyond two, no statistically significant differences from either the single or the double dive incidence values were found for flow-volume parameters. Regression slopes of flow-volume parameter changes against dive number were not significantly different from zero (Fig. 5–8).

Decreases in D_LCO below threshold were statistically more frequent after nine dives than after one through five dives. More data are needed to have much confidence in the dichotomous above/below threshold estimates, as is evident from the confidence intervals in Table 4. However, not only was the average regression slope of D_LCO vs. dive number significantly less than zero for the divers who performed eight or more dives, but that for all dives performed on two or more consecutive days (Fig. 9) also indicated a steady decrease in diffusing capacity. The slope of D_LCO vs. dive day when two or more dives were done was $-0.54\%/day$, $SE\ 0.09\%/day$, $p < 0.001$.

Four-hour dives at this partial pressure appear to be tolerable in the long term. Interestingly, the daily oxygen exposure of these dives is just slightly higher than the average daily dose that investigators who described nitrogen-oxygen saturation diving procedures postulated to be tolerable indefinitely.¹⁰

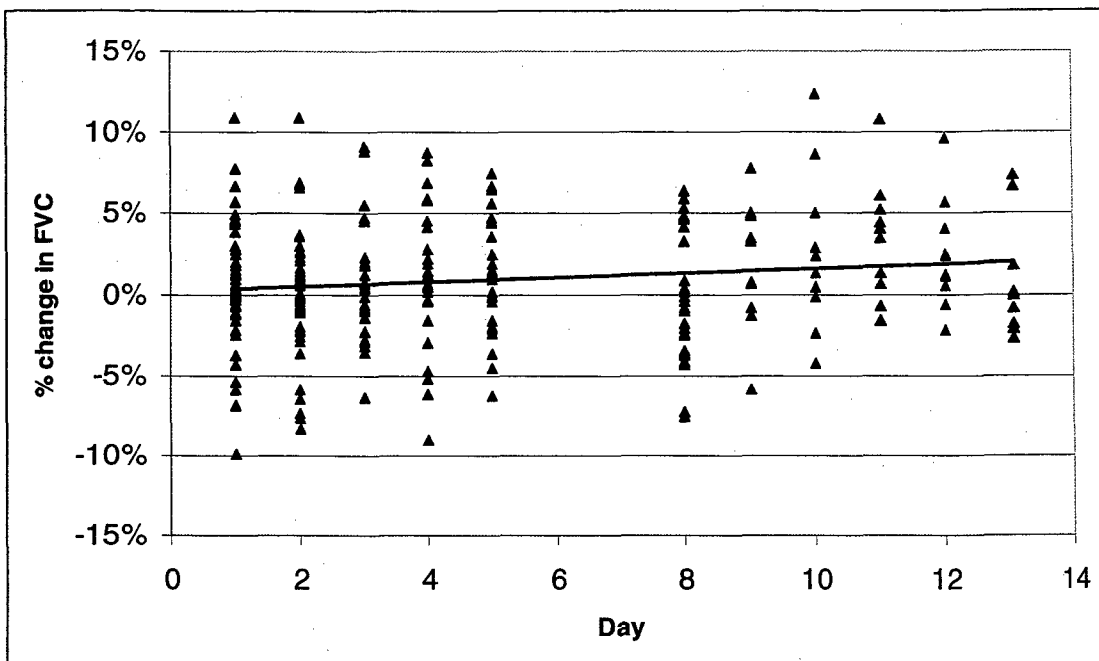


Figure 5. Changes in FVC with increasing numbers of dives. Each point represents a measurement from a diver who performed at least two consecutive dives. Numbers of data decrease as numbers of dives increase. The first-order linear regression line is shown. The slope is not different from zero.

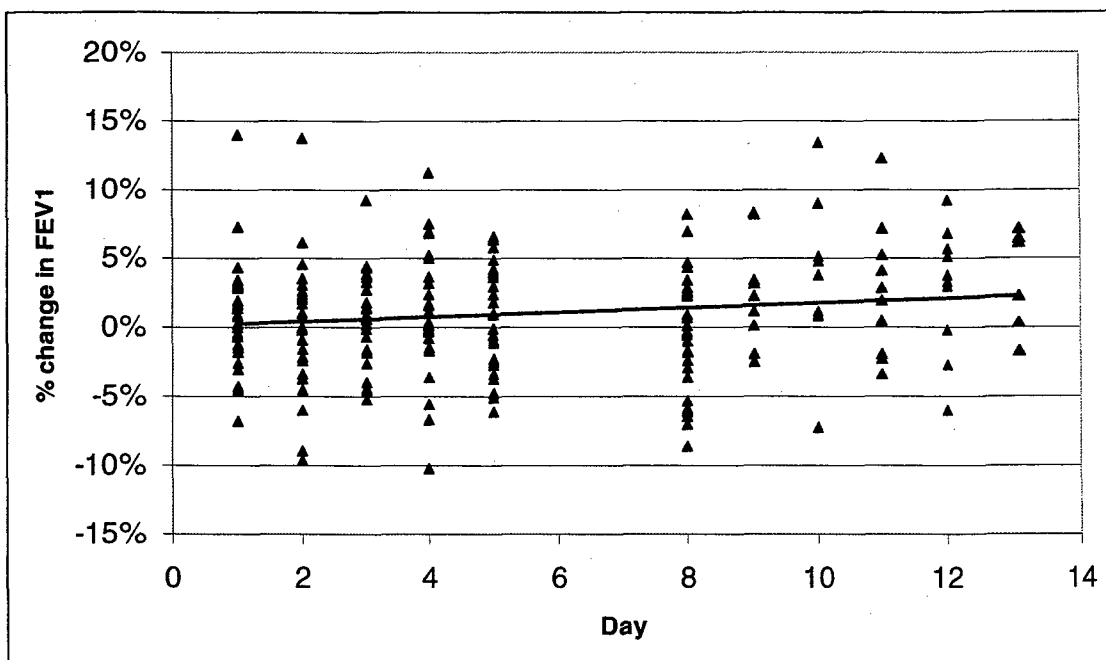


Figure 6. Changes in FEV_1 with increasing number of dives. Points and line as in Figure 5. The slope is not different from zero.

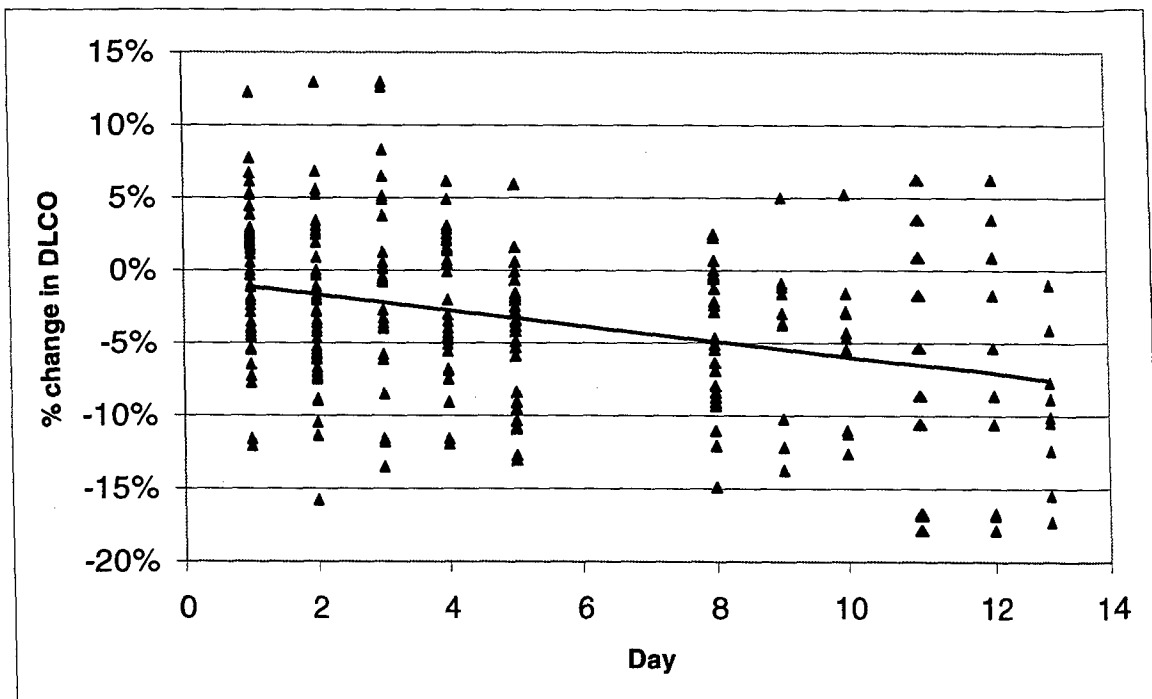


Figure 9. Changes in D_{LCO} with increasing number of dives. Points and line as in Figure 5. The slope, $-0.5\%/day$, is significantly less than zero ($p < 0.001$).

CONCLUSIONS

Divers are able to repeat 4-hour dives with an oxygen partial pressure of 1.4 atm daily for two working weeks without undue risk of pulmonary oxygen toxicity. The risk of symptoms is the same every day, and the risk of reducing FVC, FEV_1 , or another parameter of forced expiration does not increase after the second day. Changes can be expected to be mild. Diffusing capacity decreases slowly on the average, but the large normal variability in this parameter makes this result more of academic than of practical interest unless dives are to be repeated for many days. Four-hour dives performed while breathing 1.4 atm oxygen do not cause undue fatigue or exercise intolerance.

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